

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Alkaloids and Anthraquinones from Malaysian Flora

Nor Hadiani Ismail, Asmah Alias and Che Puteh Osman
Universiti Teknologi MARA,
Malaysia

1. Introduction

The flora of Malaysia is one of the richest flora in the world due to the constantly warm and uniformly humid climate. Malaysia is listed as 12th most diverse nation (Abd Aziz, 2003) in the world and mainly covered by tropical rainforests. Tropical rainforests cover only 12% of earth's land area; however they constitute about 50% to 90% of world species. At least 25% of all modern drugs originate from rainforests even though only less than 1% of world's tropical rainforest plant species have been evaluated for pharmacological properties (Kong, *et al.*, 2003). The huge diversity of Malaysian flora with about 12 000 species of flowering plants offers huge chemical diversities for numerous biological targets. Malaysian flora is a rich source of numerous class of natural compounds such as alkaloids, anthraquinones and phenolic compounds. Plants are usually investigated based on their ethnobotanical use. The phytochemical study of several well-known plants in folklore medicine such as *Eurycoma longifolia*, *Labisia pumila*, *Andrographis paniculata*, *Morinda citrifolia* and *Phyllanthus niruri* yielded many bioactive phytochemicals. This review describes our work on the alkaloids of *Fissistigma latifolium* and *Meiogyne virgata* from family Annonaceae and anthraquinones of *Renellia* and *Morinda* from Rubiaceae family.

2. The family Annonaceae as source of alkaloids

Annonaceae, known as *Mempisang* in Malaysia (Kamarudin, 1988) is a family of flowering plants consisting of trees, shrubs or woody lianas. This family is the largest family in the Magnoliales consisting of more than 130 genera with about 2300 to 2500 species. Plants of the family Annonaceae are well known as source of a variety of alkaloids (Cordell, 1981). Many alkaloids have important physiological effects on human and exhibit marked pharmacological activity which is useful as medicine. For examples, atropine is used widely as an antidote to cholinesterase inhibitors such as physostigmine. Morphine and codeine are narcotic analgesics and antitusive agent while caffeine, which occurs in coffee, tea and cocoa is a central nervous system stimulant. Caffeine is also used as cardiac and respiratory stimulant and besides as an antidote to barbiturate and morphine poisoning (Parker, 1997). The first report on phytochemical studies of alkaloids from Malaysian Annonaceae plants was on the leaves of *Desmos dasymachalus* which has led to the isolation of new 7-hydroxyaporphine, dasymachaline (Chan & Toh, 1985).

The phytochemical investigation of Malaysian Annonaceous plants for their alkaloidal content continue to flourish. Phytochemical survey of the flora of the Peninsula Malaysia and Sabah, with systematic screening for alkaloids resulted in reports on chemical constituents of several plants from Annonaceae illustrating great interest in this field (Teo, *et al.*, 1990). Lavault *et al.*, (1981) analysed the alkaloid content of three Annonaceae plants; *Disepalum pulchrum*, *Polyalthia macropoda* and *Polyalthia stenopetala* which led to the isolation of several isoquinoline compounds. Isolation of two new 7,7'-bisdehydroaporphine alkaloids; 7,7'-bisdehydro-O-methylisopiline and 7-dehydronornuciferine-7'-dehydro-O-methylisopiline from bark of *Polyalthia bullata* was reported by Connolly *et al.*, (1996). Kam (1999) reviewed the alkaloids derived from Malaysian flora in a book entitled chemical and biological approach of alkaloids.

In Malaysia, eight species of *Fissistigma* are known. They are *F. mobiforme*, *F. cylindrium*, *F. fulgens*, *F. kingii*, *F. lanuginosum*, *F. latifolium*, *F. munubriatum* and *F. kinabaluensis* (Nik Idris *et al.*, 1994). Not much has been reported on the phytochemical studies of *Fissistigma* species. The studies on the alkaloids from *Fissistigma fulgens* have led to the isolation of aporphine, oxoaporphine and protoberberine alkaloids. Liriodenine, anonaine, argentinine, discretamine and kikemanine were found from this species (Awang, *et al.*, 2000). The phytochemical work on alkaloidal composition of the Malaysian *Fissistigma manubriatum* by Saaïd and Awang (2005) yielded two oxoaporphines, lanuginosine and liriodenine together with two tetrahydroprotoberberines, tetrahydropalmatine and discretine. We studied the alkaloids of *Fissistigma latifolium* and reported the isolation of nine alkaloids including a new aporphine compound (Alias *et al.*, 2010).

Meiogyne cylindrocarpa, *Meiogyne monosperma* and *Meiogyne virgata* are the only three *Meiogyne* species found in Malaysia. Only *Meiogyne virgata* was studied by Tadic *et al.* (1987). The sample collected from Mount Kinabalu, Sabah was reported to contain azafluorene alkaloid, kinabaline, together with liriodenine, cleistopholine and other aporphine alkaloids. Our work on *Meiogyne virgata* from Hulu Terengganu yielded nine alkaloids from aporphine, oxoaporphines and azaanthracene groups.

2.1 Alkaloids of *Fissistigma latifolium* and *Meiogyne virgata*

Since the last three decades, a large number of alkaloidal compounds have been isolated from some Annonaceae species. Tertiary and quaternary isoquinoline and quinoline alkaloids are pharmacologically important compounds commonly found in Annonaceae plants. Continuing our interest on this family of plants, we pursued phytochemical investigation on *Fissistigma latifolium* and *Meiogyne virgata*.

2.1.1 Alkaloids of *Fissistigma latifolium*

Fissistigma latifolium (Dunal) Merr. from the genus *Fissistigma* is a climbing shrub found in lowland forest of Malaysia, Sumatra, Borneo and Philippines (Verdout, 1976). The genus *Fissistigma* (Annonaceae) consists of about 80 species and is widely distributed in Asia and Australia (Sinclair, 1955). Several species of the genus *Fissistigma* have been used in Southeast Asia as traditional medicines (Perry, 1980). They have been used for muscular atrophy, hepatomegaly and hepatosplenomegaly (Kan, 1979). In Malaysia, the medicinal uses of *Fissistigma* species was briefly mentioned by Burkill as the treatment for childbirth, malaria, wounds, ulcer and rheumatism (Kamarudin, 1988).

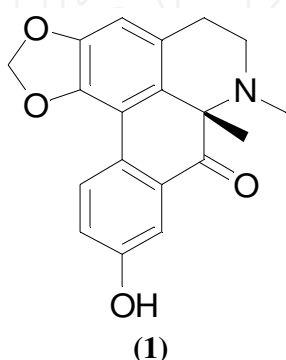


Fig. 1. *Fissistigma latifolium*

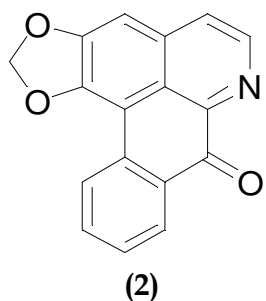
Previous studies on *F. fulgens* and *F. manubriatum* have resulted in the isolation of aporphine, oxoaporphine and protoberberine alkaloids. Similarly, the studies on alkaloids from *Fissistigma latifolium* led to the isolation of a new aporphine alkaloid, (-)-*N*-methylguattescidine **1** (Alias, *et al.*, 2010). This alkaloid, together with eight known alkaloids, namely liriodenine **2**, lanuginosine **3**, (-)-asimilobine **4**, dimethyltryptamine **5**, (-)-remerine **6**, (-)-anonaine **7**, columbamine **8** and lysicamine **9**, were obtained from the methanol extract of the bark of the plant. The new compound was characterized by analysis of spectroscopic methods such as NMR (Nuclear Magnetic Resonance), IR (Infrared) and GC-MS (Gas-Chromatography-Mass Spectrometry).

(-)-*N*-Methylguattescidine **1** exhibited a molecular formula of $C_{19}H_{17}O_4N$ based on the HRESIMS spectrum (positive mode), which showed a pseudomolecular ion at m/z 324.3581 $[M+H]^+$ (calcd. 324.3595). The UV spectrum showed an absorption band at 310 nm, suggesting the compound was an aporphine alkaloid with substitutions at position 1 and 2. The IR spectrum indicated the presence of C-H aromatic at 3056, C-O at 1266 and OH at 3409 cm^{-1} , respectively. The absorption of methyl group appeared at 2945 and 2833. The ^{13}C -NMR spectrum showed presence of 19 carbons. The signal at δ 198.0 ppm confirmed the presence of the carbonyl group, while the signal at δ 153.1 ppm is evidence for the oxygenated aromatic carbon. The DEPT spectrum revealed three methylene carbons at δ 26.9 ppm, 41.4 ppm and 96.9 ppm. Signal at δ 96.9 ppm is indicative of a methylenedioxy carbon. This is consistent with two doublets at δ 5.99 ppm ($J = 1.2$ Hz) and δ 6.07 ppm ($J = 1.2$ Hz) in the 1H -NMR spectrum for the protons of methylenedioxy group which is typically located at positions 1 and 2. The characteristic ABD aromatic signals of H-11, H-10 and H-8 of aporphine alkaloid were observed at δ 8.24 ppm (d , $J = 8.7$ Hz), δ 7.13 ppm (dd , $J = 8.7, 2.7$ Hz) and δ 7.39 ppm (d , $J = 2.7$ Hz), respectively. The 1H -NMR spectrum also exhibited an *N*-methyl signal at δ 2.34 ppm and another methyl group attached to C-6a gave a singlet at δ 1.52 ppm. The assignment of this methyl group at the 6a position is confirmed through its HMBC correlation with C-6a at δ 62.7 ppm, C-1b at δ 118.3 ppm and C-7 at δ 198.0 ppm. HMQC spectrum shows two cross peaks at δ 26.9 ppm (C-4) axis, represented the correlations of C-4 to H-4 (δ 2.55 ppm) and H-4' (δ 3.00 ppm). At δ 41.4 ppm (C-5) axis, two

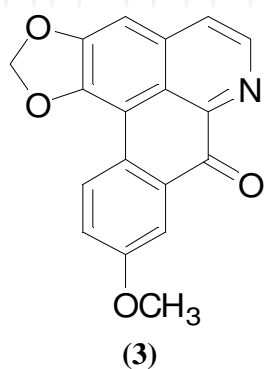
cross peaks showed the correlations between C-5 and H-5 (δ 2.99 ppm) and H-5' (δ 3.01 ppm). The quaternary carbon signals were assigned based on HMBC experiment. C-1a at δ 108.9 ppm, C-7a at δ 126.0 ppm and C-9 at δ 153.1 ppm were assigned based on their correlations with H-11 at δ 8.24 ppm, while C-1b at δ 118.3 ppm and C-2 at δ 143.2 ppm showed correlations with H-3 at δ 6.54 ppm. (-)-N-methylguattescidine, is a rare 6a-methylated-7-oxo-aporphine alkaloid, having only been previously reported by Reynald *et al.* in 1982. Presented below are structures and spectroscopic data of the isolated compounds.



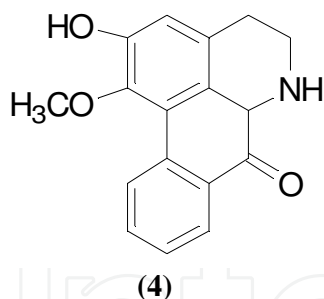
(-)-N-Methylguattescidine (**1**), yellow amorphous solid; $[\alpha]^{30}_D$: -20° ($c = 0.1 \text{ mg mL}^{-1}$, CHCl_3); MS m/z : 324.1242, $\text{C}_{19}\text{H}_{17}\text{O}_4\text{N}$; UV λ_{max} nm EtOH: 235, 310; IR ν_{max} cm^{-1} : 3409, 1710, 1266; ^1H NMR (CDCl_3 , 300 MHz) δ ppm : 8.24 (1H, d, $J = 8.7 \text{ Hz}$, H-11), 7.39 (1H, d, $J = 2.7 \text{ Hz}$, H-8), 7.13 (1H, dd, $J_o = 8.7 \text{ Hz}$; $J_m = 2.7 \text{ Hz}$, H-10), 6.54 (1H, s, H-3), 6.07 (1H, d, $J = 1.2 \text{ Hz}$, H-2), 5.99 (1H, d, $J = 1.2 \text{ Hz}$, H-1), 3.52 (1H, m, H-11a), 3.01 (1H, m, H-5), 3.00 (1H, m, H-4), 2.99 (1H, m, H-5'), 2.55 (1H, m, H-4'); ^{13}C NMR (CDCl_3 , 75 MHz) δ ppm : 153.1 (C-9), 143.2 (C-2), 138.8 (C-1), 126.0 (C-7a), 125.3 (C-3a), 123.1 (C-11a), 122.7 (C-11), 122.2 (C-10), 118.3 (C-1b), 110.3 (C-8), 108.9 (C-1a), 103.9 (C-3), 96.9 (O-CH₂-O), 62.7 (C-6a), 41.4 (C-5), 34.1 (N-CH₃), 26.9 (C-4), 25.0 (CH₃).



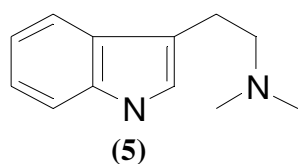
Liriodenine (**2**), yellow needles; MS m/z : 275, $\text{C}_{17}\text{H}_9\text{O}_3\text{N}$; UV λ_{max} nm EtOH : 215, 246, 268, 395, 412; IR ν_{max} cm^{-1} : 3054, 1726, 1421, 1265; ^1H NMR (CDCl_3 , 300 MHz) δ ppm : 8.9 (1H, d, $J = 5.1 \text{ Hz}$, H-5), 8.66 (1H, dd, $J_o = 7.2 \text{ Hz}$; $J_m = 1.2 \text{ Hz}$, H-11), 8.59 (1H, dd, $J_o = 7.8 \text{ Hz}$; $J_m = 1.2 \text{ Hz}$, H-8), 7.79 (1H, d, $J = 5.1 \text{ Hz}$, H-4), 7.76 (1H, td, $J_o = 7.8 \text{ Hz}$; $J_m = 1.5 \text{ Hz}$, H-10), 7.59 (1H, td, $J_o = 7.8 \text{ Hz}$; $J_m = 1.2 \text{ Hz}$, H-9), 7.16 (1H, s, H-3), 6.40 (2H, s, O-CH₂-O); ^{13}C NMR (CDCl_3 , 75 MHz) δ ppm : 151.7 (C-2), 147.9 (C-1), 146 (C-6a), 145.4 (C-3a), 144.9 (C-5), 135.7 (C-1a), 133.9 (C-10), 132.9 (C-7a), 131.3 (C-11a), 128.8 (C-8), 128.6 (C-9), 127.4 (C-11), 124.2 (C-4), 108.2 (C-1b), 103.3 (C-3), 102.4 (O-CH₂-O), 182.4 (C-7).



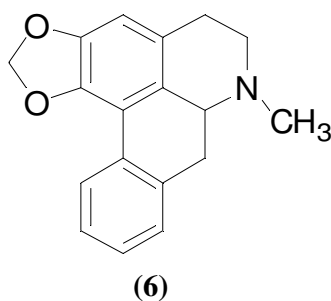
Lanuginosine (**3**), yellow needles; MS m/z : 305, $\text{C}_{18}\text{H}_{11}\text{O}_4\text{N}$; UV λ_{max} nm EtOH : 246, 271, 315, 258, 283, 334; IR ν_{max} cm^{-1} : 3055, 2987, 2306, 1712, 1635, 1363, 1265, 1046, 896; ^1H NMR (CDCl_3 , 300MHz) δ ppm : 8.85 (1H, d, $J = 5.4 \text{ Hz}$, H-5), 8.58 (1H, d, $J_o = 9.0 \text{ Hz}$, H-11), 8.04 (1H, d, $J = 3 \text{ Hz}$, H-8), 7.79 (1H, d, $J = 5.4 \text{ Hz}$, H-4), 7.32 (1H, dd, $J_o = 9.0 \text{ Hz}$; $J_m = 3 \text{ Hz}$, H-10), 7.17 (1H, s, H-3), 6.47 (2H, s, O - CH₂ - O); ^{13}C NMR (CDCl_3 , 75MHz) δ ppm : 158.0 (C-9), 151.0 (C-2), 146.0 (C-1), 144.9 (C-5), 144.0 (C-6a), 136.0 (C-3a), 133.0 (C-7a), 131.9 (C-1b), 129.1 (C-11), 126.2 (C-11a), 124.3 (C-4), 122.6 (C-10), 110.2 (C-8), 109.0 (C-1a), 102.3 (C-3), 55.8 (OCH₃), 102.5 (O - CH₂ - O), 182.0 (C-7).



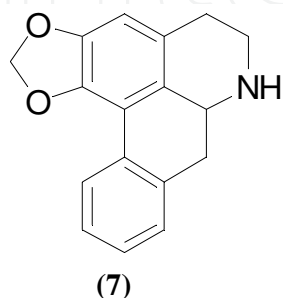
Asimilobine (4), brownish amorphous; MS m/z : 267, $C_{17}H_{17}O_2N$; UV λ_{max} nm EtOH : 274, 308; IR ν_{max} cm^{-1} : 3390, 1675, 1600, 1225; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 8.30 (1H, d, $J = 7.8$ Hz, H-11), 7.36 – 7.25 (3H, m, H-8, H-9, H-10), 6.73 (1H, s, H-3), 3.92 (1H, m, H-6a), 3.50 (1H, m, H-5'), 3.08 (1H, d, H-4'), 3.04 (1H, d, H-5), 2.99 (1H, m, H-7), 2.85 (1H, m, H-7), 2.74 (1H, d, H-4), 3.61 (3H, s, OCH_3), 2.00 (1H, s, N-H); ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 148.6 (C-2), 143.0 (C-1), 135.6 (C-7a), 131.7 (C-11a), 129.4 (C-16), 128.1 (C-3a), 127.7 (C-8), 127.4 (C-10), 127.3 (C-9), 127.2 (C-11), 125.5 (C-1a), 114.6 (C-3), 53.4 (C-6a), 42.8 (C-5), 36.7 (C-7), 28.2 (C-4), 60.4 (OCH_3).



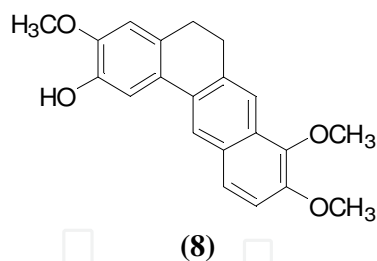
Dimethyltryptamine (5), reddish amorphous; MS m/z : 188, $C_{12}H_{16}N_2$; UV λ_{max} nm EtOH : 240, 252; IR ν_{max} cm^{-1} : 3945, 3055, 2305, 1634, 1422, 1265, 1046, 896; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 7.60 (1H, d, $J_o = 5.7$ Hz, H-7), 7.38 (1H, d, $J_o = 7.1$ Hz, H-4), 7.20 (1H, td, $J_o = 6.9$ Hz; $J_m = 0.9$ Hz, H-5), 7.12 (1H, td, $J_o = 6.9$ Hz; $J_m = 0.9$ Hz, H-6), 3.03 (2H, m, H-8), 2.80 (2H, m, H-9), 8.28 (1H, brs, N-H), 2.49 (6H, s, $2(CH_3)$); ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 136.0 (C-7), 127.0 (C-3a), 122.0 (C-6), 121.7 (C-2), 119.2 (C-5), 118.7 (C-4), 59.4 (C-9), 44 (C-3), 22.9 (C-8), 44.9 ($2CH_3$).



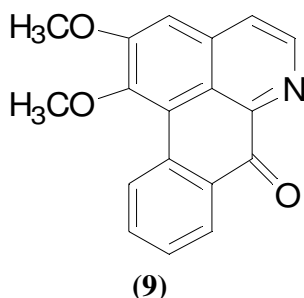
Remerine (6), yellow amorphous; MS m/z : 279, $C_{18}H_{17}O_2N$; UV λ_{max} nm EtOH : 234, 264; IR ν_{max} cm^{-1} : 1401, 1361, 1053, 942; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 8.09 (1H, d, $J_o = 7.5$ Hz, H-11), 7.34 – 7.24 (3H, m, H-8, H-9, H-10), 6.59 (1H, s, H-3), 4.000 (1H, m, H-6a), 3.4 (1H, m, H-5'), 3.10 (1H, m, H-4'), 3.00 (1H, m, H-5), 2.90 (1H, m, H-7'), 2.80 (2H, m, H-7, H-4), 6.11 (1H, d, $J_m = 1.2$ Hz, CH-O), 5.96 (1H, d, $J_o = 1.2$ Hz, CH-O), 2.62 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 146.7 (C-2), 142.8 (C-1), 136.3 (C-7a), 128.1 (C-8), 128.0 (C-1b), 127.6 (C-9), 127.0 (C-10), 127.0 (C-11), 125.4 (C-3a), 126.5 (C-1a), 126.0 (C-11a), 125.4 (C-3a), 62.4 (C-6a), 53.3 (C-6a), 43 (C-5), 36.9 (C-7), 28 (C-4), 100.7 (O – CH_2 – O), 39.0 (CH_3).



Anonaine (7), yellow amorphous; MS m/z : 265, $C_{17}H_{13}O_2N$; UV λ_{max} nm EtOH : 234, 272, 315; IR ν_{max} cm^{-1} : 1040, 945; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 8.09 (1H, d, $J_o = 7.5$ Hz, H-11), 7.36 – 7.19 (3H, m, H-8, H-9, H-10), 6.6 (1H, s, H-3), 4.04 (1H, dd, H-6a), 3.48 (1H, m, H-5'), 3.1 (1H, m, H-4'), 3.07 (1H, m, H-5), 3.02 (1H, m, H-7'), 6.12 (1H, d, $J_m = 1.5$, CH – O), 5.97 (1H, d, $J_m = 1.5$, CH – O); ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 147.0 (C-2), 143.0 (C-1), 135.4 (C-7a), 131.4 (C-11a), 129.0 (C-1b), 128.0 (C-3a), 127.8 (C-8), 127.7 (C-9), 127.0 (C-10), 126.1 (C-11), 116.3 (C-1a), 53.6 (C-6a), 43.6 (C-5), 37.4 (C-7), 29.6 (C-4), 100.6 (O – CH_2 – O).



Columbamine (**8**), red amorphous solid; MS m/z : 338, $C_{20}H_{20}O_4N$; UV λ_{max} nm EtOH : 206, 225, 265, 345; IR ν_{max} cm^{-1} : 3390, 1600; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 9.00 (1H, s, H-8), 8.08 (1H, s, H-13), 7.65 (1H, d, $J_o = 9.0$ Hz, H-11), 7.61 (1H, d, $J_o = 8.7$ Hz, H-12), 7.27 (1H, s, H-1), 6.79 (1H, s, H-4), 4.68 (2H, t, $J_o = 6.6$ Hz; 6.3 Hz, H-6), 3.18 (2H, t, $J_o = 6.0$ Hz, H-5), 4.02 (3H, OCH_3), 3.99 (3H, OCH_3), 3.92 (3H, OCH_3). ; ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 163.0 (C-10), 151.0 (C-3), 150.0 (C-4a), 149.0 (C-2), 142.0 (C-9), 140.0 (C-8), 139.0 (C-11), 132.0 (C-14), 129.0 (C-12a), 126.0 (C-1a), 123.3 (C-12), 120.0 (C-13), 119.0 (C-8a), 111.0 (C-4), 108.0 (C-1), 56.0 (C-6), 27.0 (C-5), 60.0 (OCH_3), 58.0 (OCH_3), 57.0 (OCH_3).



Lysicamine (**9**), yellow amorphous; MS m/z : 291, $C_{18}H_{13}O_3N$; UV λ_{max} nm EtOH : 214, 250, 255, 261, 319; IR ν_{max} cm^{-1} : 1675, 1600, 1225; 1H NMR ($CDCl_3$, 300MHz) δ ppm : 9.10 (1H, d, $J_o = 5.1$ Hz, H-11), 8.70 (1H, d, $J_o = 6.9$ Hz, H-5), 8.48 (1H, dd, $J_o = 7.5$ Hz; $J_m = 1.5$ Hz, H-8), 7.76 (1H, td, $J_o = 7.2$ Hz; $J_m = 1.5$ Hz, H-10), 7.7 (1H, d, $J_o = 6.9$ Hz, H-4), 7.55 (1H, td, $J_o = 7.2$ Hz; $J_m = 1.2$ Hz, H-9), 7.24 (1H, s, H-3), 4.05 (3H, s, OCH_3), 3.97 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm : 156.7 (C-6a), 152.0 (C-2), 145.2 (C-1), 139.0 (C-5), 135.3 (C-3a), 134.7 (C-11a), 132.0 (C-7a), 130.9 (C-10), 125.7 (C-9), 122.0 (C-1b), 119.6 (C-1a), 108.7 (C-3), 65.1 (OCH_3), 56.8 (OCH_3), 182.5 (C=O).

Table 1.

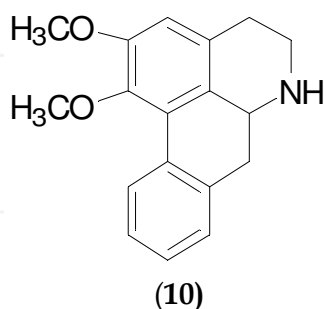
2.1.1 Alkaloids of *Meiogyne virgata*

Meiogyne virgata is a rainforest tree grows in Peninsular Malaysia, Borneo, Java and Sumatera. The genus *Meiogyne* (Annonaceae) consists of about 24 species and widely distributed in Indo-china, Thailand, Peninsular Malaysia, Sumatra, Java, Borneo and the Philippines. There is no formal report on the traditional uses of *Meiogyne virgata* in Malaysia. However, being an alkaloid rich species, it could be useful medicinally.

We have conducted phytochemical work on *Meiogyne virgata*. Six of the aporphine alkaloids in *Fissistigma latifolium* were also found in *Meiogyne virgata* collected from the Peninsular Malaysia. Isolation and purification of alkaloids from the bark of *Meiogyne virgata* afforded nine alkaloids; four oxoaporphines, liriodenine **2**, lanuginosine **3**, asimilobine **4** and lysicamine **9**; four aporphines, anonaine **7**, remerine **6**, nornuciferine **10** and norushinsunine **11**; and one azaanthracene alkaloid, cleistopholine **12**.

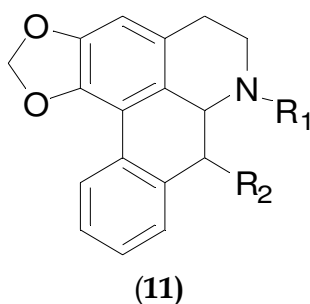
Most of the compounds are yellowish or colorless hygroscopic liquid at room temperature while impure samples will appear brownish. They have low solubility in water but dissolve well in methanol, chloroform, acetone, dichloromethane and other common organic solvent. They are also soluble in dilute acid as the protonated derivative. The melting point of these type of compounds in range 100-300 °C.

Most of oxoaporphine and aporphine alkaloids showed IR spectra typified by the 7-oxo group with absorption band in the 1635-1660 cm^{-1} region. The UV spectra data for these type of compounds are quite characteristic for the skeletal type. There is indication that they may also be diagnostic for a particular oxygenation pattern. For example, 1, 2-methylenedioxy

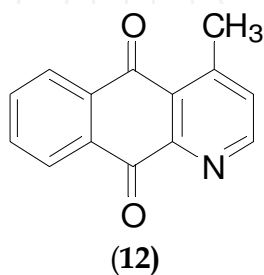


Nornuciferine (**10**), Colourless crystalline solid; MS m/z : 281 (M^+); UV λ_{max} nm EtOH : 234, 272, 315; IR ν_{max} cm^{-1} : 1040, 945

^1H NMR (CDCl_3 , 300 MHz) δ ppm : 8.39 (1H, d , J = 7.8 Hz, H-11), 7.33-7.20 (3H, m , H-8, H-9, H-10), 6.65 (1H, s , H-3), 3.98 (1H, dd , J = 13.4; 5.2 Hz, H-6a), 3.41 (1H, dd , J = 12.3; 6.3 Hz, H-5'), 3.90 (3H, s , OMe-2), 3.68 (3H, s , OMe-1), 3.08 (1H, dd , J =13.2 Hz, H-4), 3.04 (1H, td , J = 12.3; 5.1 Hz, H-5), 2.85 (1H, dd , J = 13.4 ; 5.2 Hz, H-7'), 2.68 (1H, dd , J = 13.2; 6.0 Hz, H-4'), 2.64 (1H, t , J = 13.4 Hz, H-7).; ^{13}C NMR (CDCl_3 , 125 MHz) δ ppm : 152.3 (C-2), 145.2 (C-1), 135.0 (C-7a), 132.1 (C-1b), 132.1 (C-11a), 131.2 (C-3a), 128.4 (C-8), 127.8 (C-10), 127.4 (C-9), 127.1 (C-11), 126.6 (C-1a), 111.8 (C-3), 60.3 (OMe-1), 55.9 (OMe-2), 53.6 (C-6a), 43.0 (C-5), 37.2 (C-7), 29.7 (C-4).



Norushinsunine (**11**), Colourless crystalline solid; MS m/z : 281; UV λ_{max} nm EtOH : 217, 247, 252, 259, 273, 319; IR ν_{max} cm^{-1} : 3488, 3355, 1574, 1215; ^1H NMR (CDCl_3 , 300MHz) δ ppm : 8.16 (1H, dd , J = 7.2;1.2 Hz, H=11), 7.45 (1H, td , J = 8.7;1.2 Hz, H-10), 7.40 (1H, dd , J = 8.1;0.9 Hz, H-8), 7.34 (1H, td , J = 7.2;1.2 Hz, H-9), 6.59 (1H, s , H-3), 6.11 (1H, d , J =1.5 Hz, O - CH_2 - O), 5.95 (1H, d , J = 1.2 Hz, O - CH_2 - O), 4.61 (1H, d , J = 3.0 Hz, H-7), 4.06 (1H, d , J = 3.3 Hz, CH - O). 3.37 (1H, ddd , J = 5.0;3.9;1.2 Hz, H-4', 2.68 (1H, dd , J =16.2;3.9 Hz, H-4); ^{13}C NMR (CDCl_3 , 75MHz) δ ppm : 147.1 (C-1), 142.6 (C-2), 135.6 (C-1a), 130.3 (C-7a), 129.4 (C-9), 129.1 (C-3a), 123.6 (C-1b), 115.6 (C-11a), 108.4 (O - CH_2 - O), 71.0 (C-7), 57.2 (C-6a), 43.1 (C-5), 29.2 (C-4).



Cleistopholine (**12**), yellow glassy solid; MS m/z : 281 (M^+); UV λ_{max} nm EtOH : 234, 272, 315; IR ν_{max} cm^{-1} : 1040, 945; ^1H NMR (CDCl_3 , 400 MHz) δ ppm : 8.95 (1H, d , J = 4.8 Hz, H-2), 8.31 (1H, dd , J = 8.5;2.2 Hz, H-5), 8.21 (1H, dd , J = 8.5;2.2 Hz, H-8), 7.79 (1H, m , H-6), 7.79 (1H, m , H-7), 2.89 (1H, s , CH_3); ^{13}C NMR (CDCl_3 , 100.6 MHz) δ ppm : 184.7 (C-9), 181.9 (C-10), 153.4 (C-2), 151.6 (C-4), 150.1 (C-9a), 134.6 (C-7), 134.2 (C-6), 132.6 (C-10a), 131.2 (C-3), 129.1 (C-4a), 127.4 (C-5), 127.2 (C-8), 22.8 (CH_3).

Table 2.

derivative in compound **2** gives increase to a bathochromic shift in the 235-250 nm bands on comparison with the corresponding compound **9**. The addition of acid will give a substantial bathochromic shift of the longest-wavelength band. In oxoaporphine and aporphine, position 1 and 2 are constantly oxygenated. It is frequent to find further oxygen substituent at C-9, C-10 and C-11 and occasionally at C-8. Other than that, H-4 and H-5 will give a characteristic AB system with doublet of doublet at about 7.6 ppm and 8.7 ppm with a coupling constant about 5.4 Hz. The small *J* value is due to the adjacent of electronegative nitrogen atom. The methylenedioxy group gives singlet peak at about 6.0 ppm due to the inductive effect caused by existence of the neighboring C-7 carbonyl. The C-11 proton usually the most deshielded and the C-3 protons always appeared at a higher field than the aromatic hydrogen (Cordell, 1981). Presented below are structures and spectroscopic data of the isolated compounds.

3. The family of Rubiaceae as source of anthraquinones

Rubiaceae is among the largest flowering plants family comprising of 450 genera and 13,000 species. In Malaysia, 70 genera and 555 species of Rubiaceae plants were reported (Wong, 1989). Most Rubiaceae plants are shrubs or small trees and infrequently herbs (Hutchinson, 1973). Rubiaceae plants are distributed worldwide but they are mainly tropical. They are easily recognized at family level by decussate, entire leaves, presence of stipules, actinomorphic flowers and inferior ovary.

Rubiaceae plants are known to accumulate substantial amount of anthraquinones particularly in the roots (Han, *et al.*, 2001). Anthraquinones containing plants are used traditionally for various ailments and health complaints such as diarrhea, loss of appetite, fever, wounds and cancer. The plant extracts are used in form of poultice, lotion and decoction from various plant parts. *Morinda*, *Hedyotis*, *Prismatomeris* and *Rennellia* are among anthraquinone containing genera that are widely used in Malaysian traditional medicine (Ismail, *et al.*, 1997; Jasril, *et al.*, 2003; Ahmad, *et al.*, 2005; Lajis, *et al.*, 2006; Osman, *et al.*, 2010).

Morinda comprises of approximately 80 species, distributed worldwide in tropical areas. It is considered to be highly nutritious plant and is used as traditional medicine. In Malaysia *M. citrifolia* and *M. elliptica* are widely used. The roots of *M. elliptica* are used to treat jaundice and gastric complaints and the leaves are used to treat flatulence and fever. *Prismatomeris* and *Hedyotis* species on the other hand are recorded in various traditional medicine systems such as Traditional Chinese Medicine. Several well-known *Prismatomeris* species used in folk medicine in Malaysia are *P. glabra* and *P. malayana*. *P. glabra* is claimed to be aphrodisiac and widely used in the east coast of Malaysia. *P. malayana* contained the anthraquinones, rubiadin and rubiadin-1-methyl ether (Lee, 1969). *Hedyotis* plants are generally consumed as tonic or febrifuge for treatment of diarrhea and dysentery (Lajis, *et al.*, 2006). Several species of *Hedyotis* native to Malaysia are *H. capitellata*, *H. herbaceae*, *H. dichtoma*, *H. diffusa* and *H. verticillata*. Besides anthraquinones, *Hedyotis* also contain β -carboline alkaloids, flavonoids and triterpenes. *Rennellia* is another small genus of Rubiaceae family. Consists of shrubs and small trees, the plants may be found in lowland tropical rainforest of Peninsular Malaysia and Sumatra. *R. elliptica*, is used for general health improvements and dubbed as Malaysian Ginseng most likely due to the appearance of its yellow roots.

Anthraquinones of the Malaysian Rubiaceae are generally of the *Rubia* type. Rings A and B of the anthraquinone skeleton are biosynthetically derived from chorismic acid and α -ketoglutarate *via* *o*-succinylbenzoic acid, whereas ring C is formed from isopentenyl diphosphate *via* the terpenoid pathway (Han, *et al.*, 2001). Chorismate is first converted to isochorismate, and then to *o*-succinylbenzoic acid (OSB) in the presence of α -ketoglutarate and thiamine diphosphate. OSB is activated at the aliphatic carboxyl group to produce an OSB-CoA ester. It is the ring closure of OSB-CoA which results in the formation of 1,4-dihydroxy-2-naphthoic acid (DHNA) leading to ring A and B. The prenylation of DHNA at C-3, leads to naphthoquinol or naphthoquinone. The ring C formation is a consequence of the cyclization *via* C-C bond between the aromatic ring of the naphthoquinone and an isoprene unit, isopentenyl diphosphate (IPP) or 3,3-dimethylallyl diphosphate (DMAPP).

Of the anthraquinone from Malaysian Rubiaceae are substituted only on ring C while the remaining are substituted on both ring A and ring C. Anthraquinones from genus *Morinda* are typically substituted at C-1, C-2, and C-5, C-6 or C-7, C-8 and C-1, C-2 and C-3

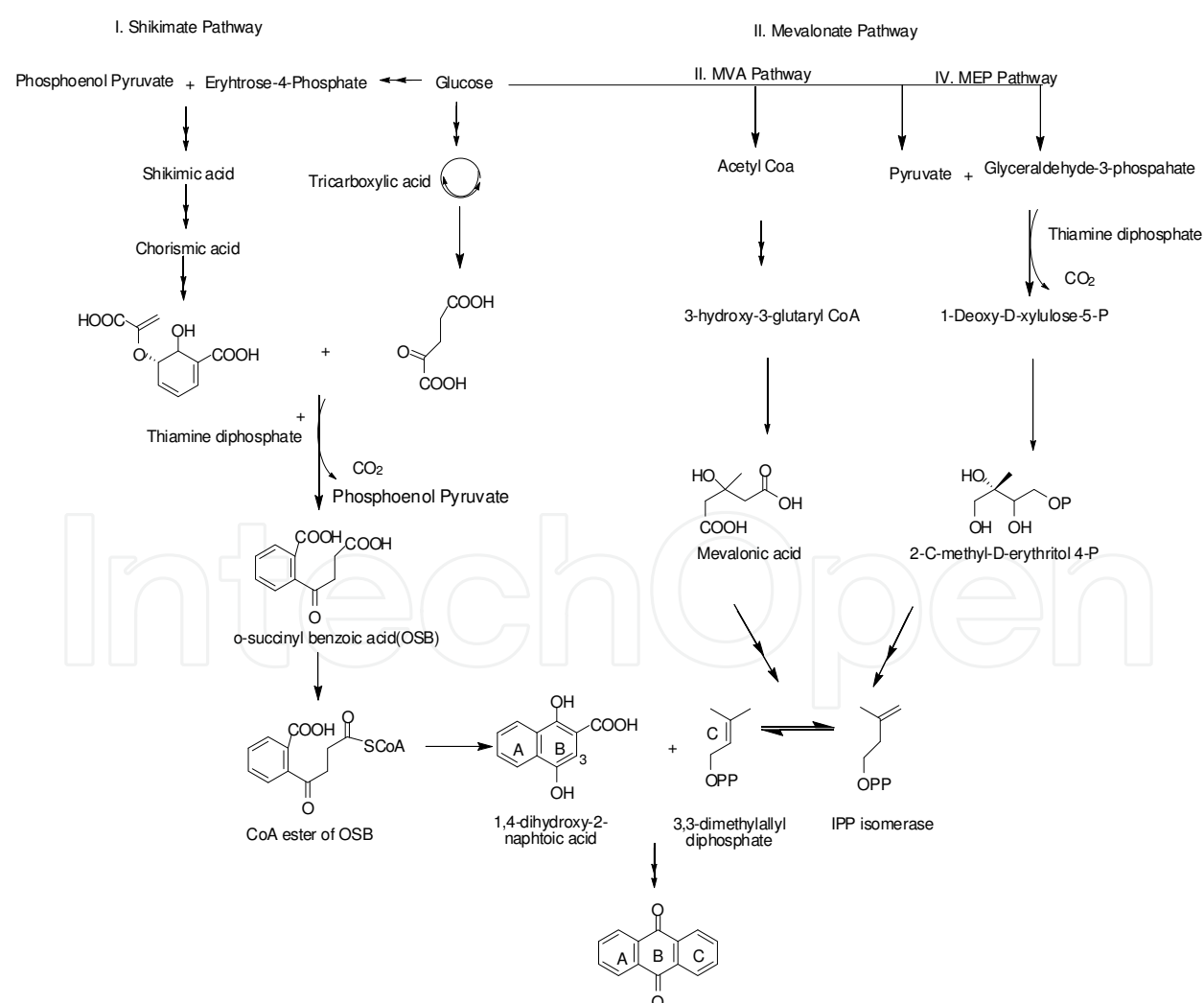


Fig. 2. Biosynthetic Pathway of Anthraquinones

meanwhile anthraquinones from *Hedyotis* are differed by rare substitution at C-1, C-2 and C-4. Anthraquinones from *Hedyotis* displayed wide structural variation. *H. capitellata* contains furanoanthraquinones (Ahmad, *et al.*, 2005) and *H. dichotoma* was reported to contain both 9,10- and 1,4-anthraquinone (Hamzah & Lajis, 1998). Genus *Rennellia* is closely related to *Morinda* and anthraquinones reported from *R. elliptica* are similar to those from genus *Morinda* (Osman *et al.*, 2010). One particular difference is the occurrence of anthraquinone with methyl substitution at C-6 which is characteristic to this plant.

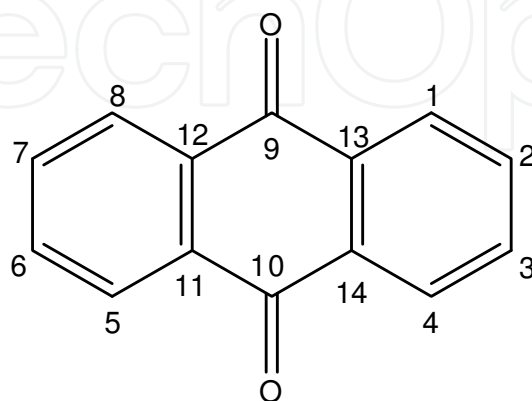


Fig. 3. Basic Skeleton of Anthraquinones

There are several characteristic spectroscopic data that distinguished anthraquinones from other types of compounds. In mass spectra, the major fragmentations are due to two consecutive loss of carbonyls, $[M-CO]^+$ and $[M-2CO]^+$. In the IR spectra, the unchelated carbonyl only viewed as one sharp stretching band at 1670 cm^{-1} due to symmetrical character of 9,10-anthraquinone (Derksen, *et al.*, 2002). Anthraquinones substituted with hydroxyl at *peri* position displayed two carbonyl absorption bands at about 1670 cm^{-1} and 1630 cm^{-1} . Anthraquinones give several characteristic UV absorptions at 265-280 nm and 285-290 nm due to electron transfers bonds of benzoid chromophore and at 430-437 nm due local excitation of quinoid carbonyls. The location hydroxyl substituent can be distinguished by observing the absorption maxima in UV spectra. Addition of dilute sodium hydroxide solution caused bathchromic shift of absorption maxima. The shift is useful in distinguishing substitution pattern of polyhydroxyanthraquinones. Proton NMR spectra of 9,10-anthraquinones shows typical A_2B_2 substitution pattern of *ortho*-substituted aromatic ring. An unsubstituted anthraquinone ring can be easily distinguished by the presence of at least two sets of multiplets at ca. δ_H 8.10 and ca. δ_H 7.20 in the aromatic region. Anthraquinones substituted at both rings A and C will give several doublets in the aromatic region. The two carbonyl groups in the molecule can be easily distinguished if hydroxyl substituents present in *para* position. Hydroxyl groups adjacent to carbonyl can be seen as sharp singlets much downfield at δ_H 12-14 due to strong intramolecular hydrogen bonding to the adjacent carbonyl. The presence of hydroxyl adjacent to carbonyl cause significant shift of carbonyl carbon resonance to downfield region at 186-189 ppm.

3.1 Anthraquinones of *Rennellia elliptica* Korth.

R. elliptica Korth. was also previously known as *R. elongata* (King & Gamble) Ridl. It is a shrub of about 2 m tall. This shrub can be found in lowland to hill forest to c. 500m above sea level. *R. elliptica* Korth. is widely distributed from Southern Myanmar to West Malaysia.

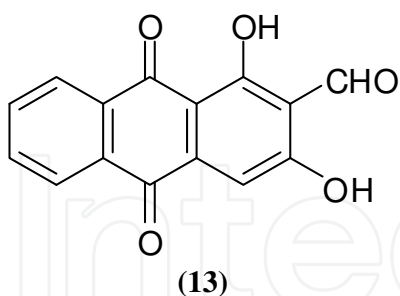
R. elliptica is used for general health improvements and dubbed as Malaysian Ginseng may be due to the appearance of its yellow roots. Its medicinal uses were documented as treatment of body aches, after-birth tonic and aphrodisiac (Mat Salleh & Latiff, 2002). The root extract of *R. elliptica* was reported to be antimalarial (Osman, *et al.*, 2010) and antioxidant (Ahmad, *et al.*, 2010). Further study is warranted to investigate the antimalarial potential of roots of *R. elliptica*.



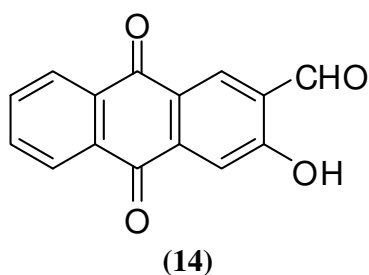
Fig. 4. *Rennellia elliptica* Korth

Phytochemical studies of the roots of *R. elliptica* Korth. resulted a new anthraquinone 1,2-dimethoxy-6-methyl-9,10-anthraquinone **18**, along with ten known ones. The known anthraquinones were nordamnacanthal **13**, 2-formyl-3-hydroxy-9,10-anthraquinone **14**, damnacanthal **15**, 1-hydroxy-2-methoxy-6-methyl-9,10-anthraquinone **16**, lucidin- ω -methyl ether **17**, 3-hydroxy-2-methoxy-6-methyl-9,10-anthraquinone **19**, rubiadin **20**, 3-hydroxy-2-methyl-9,10-anthraquinone **21**, rubiadin-1-methyl ether **22** and 3-hydroxy-2-hydroxymethyl-9,10-anthraquinone **23**.

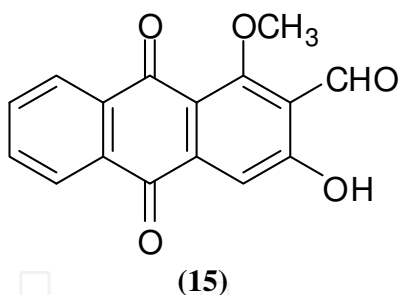
Anthraquinone **18**, 1,2-dimethoxy-6-methyl-9,10-anthraquinone, isolated for the first time as bright yellow amorphous solid. The HREIMS of **18** displayed a $[M + H]^+$ peak at 283.0968 [calc 283.3067] suggesting a molecular formula of $C_{17}H_{14}O_4$. The absorption maxima in the UV spectrum were observed at 373, 341 and 257 nm, indicative of an anthraquinone moiety. The IR spectrum did not show presence of chelated carbonyl and hydroxyl groups. The sp^2 C-H stretch for the aromatic ring was observed at $3,081\text{ cm}^{-1}$. With the exception of the sharp singlet in the downfield region for the hydrogen-bonded hydroxyl group, the ^1H NMR spectrum resembles that of compound **16**, suggesting a similar substitution pattern. Splitting pattern of the five aromatic proton signals suggested substitutions on both rings. Two overlapping doublets centered at δ_H 8.17 are due to H-8 (d , $J = 7.8\text{ Hz}$) and H-4 (d , $J = 8.7\text{ Hz}$), the *peri*-hydrogens. A doublet at δ_H 7.28 ($J = 8.7\text{ Hz}$) is due to H-3, meanwhile H-7 gave another doublet of doublet at δ_H 7.58 ($J_o = 7.8\text{ Hz}$, $J_m = 1.7\text{ Hz}$). These assignments were confirmed by their respective correlations in the COSY spectrum. H-5 resonated as a singlet at 8.06 ppm. In addition, two sharp singlets at δ_H 2.53 (3H, s) and 4.02 (6H, s) due to a methyl and two methoxy groups, respectively, were also observed. The location of the methoxy groups were established at C-1 and C-2 of ring C based on its NOE correlation with H-3. Thus, the only possible location for the methyl substituent is at C-6. This assignment was confirmed through NOE correlations of the methyl group with H-5 and H-7. The placement of methyl group at C-6 was further confirmed by HMBC experiment



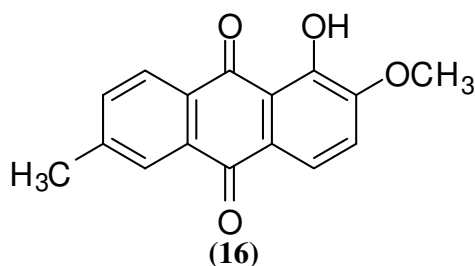
Nordamnacanthal. (13) Orange crystals. Mps 216-219 ° [lit. 220 ° C (Me₂CO) Chang (1984)]. UVλ_{max} EtOH nm: 421, 295, 259. UVλ_{max} EtOH/ -OH nm: 512, 357, 283. IR ν_{max} (KBr) cm⁻¹: 3460, 1646, 1627, 1382. MS m/z 268 [M⁺], 240, 212, 184, 138. ¹H NMR (CDCl₃, 300MHz): 14.05 (1H, s, 1-OH), 12.70 (1H, s, 3-OH), 10.52 (1H, s, 2-CHO), 8.30 (2H, m, H-5, H-8), 7.88 (2H, m, H-6, H-7), 7.36 (1H, s, H-4). ¹³C NMR (CDCl₃, 75.5 MHz): 193.9 (2-CHO), 186.8 (C=O, C-9), 181.4 (C=O, C-10), 169.2 (C-OH, C-1), 168.1 (C-OH, C-3), 139.1 (C-2), 134.8 (C-7), 134.7 (C-6), 133.3 (C-14), 133.2 (C-13), 127.8 (C-8), 127.0 (H-5), 112.1 (C-14), 109.4 (C-4), 109.1 (C-13)



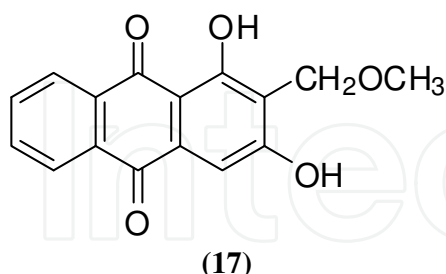
3-Formyl-2-hydroxy-9,10-anthraquinone (14). Bright orange needle crystals. Mps 212-214 °C [259-260 °C, Rath et al. (1995)]. UVλ_{max} EtOH nm: 380, 277, 246. UVλ_{max} EtOH/ -OH nm: 466, 392, 310, 254. IR ν_{max} (KBr) cm⁻¹: 3467, 1655, 1657, 1564. MS m/z 252 [M⁺], 229, 206, 167, 139. ¹H NMR (CDCl₃, 300MHz): 11.45 (1H, s, 3-OH), 10.17 (1H, s, 2-CHO), 8.68 (1H, s, H-4), 8.35 (2H, m, H-5, H-8), 7.88 (2H, m, H-6, H-7), 7.86 (1H, s, H-1). ¹³C NMR (CDCl₃, 75.5 MHz): 196.8 (2-CHO), 181.0 (C=O, C-9, C-10), 165.3 (C-OH, C-3), 139.1, 134.8 (C-4), 134.8, 133.3, 127.6, 127.5, 127.3, 126.1, 124.5, 123.4, 116.5 (C-1)



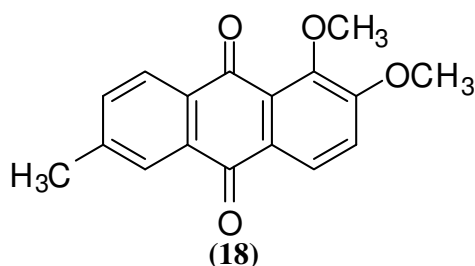
Damnacanthal (15). Yellow crystals. Mps 208-211 °C [lit. 218-218.5 ° C (Me₂CO) Chang (1984)]. UVλ_{max} EtOH nm: 381, 284, 250, 213. UVλ_{max} EtOH/ -OH nm: 460, 379, 315, 262, 250. IR ν_{max} (KBr) cm⁻¹: 3437, 1644, 1561. MS m/z: 282 [M⁺], 254, 225, 196. ¹H NMR (CDCl₃, 300MHz): 12.29 (1H, s, 3-OH), 10.49 (1H, s, 2-CHO), 8.25 (2H, m, H-5, H-8), 7.84 (2H, m, H-6, H-7), 7.68 (1H, s, H-4), 4.14 (3H, s, 1-OCH₃)



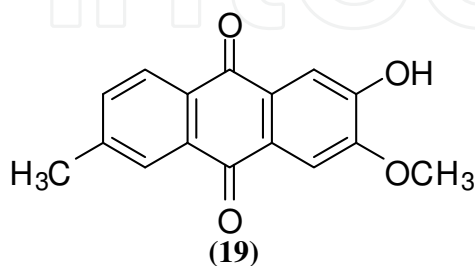
1-Hydroxy-2-methoxy-6-methyl-9,10-anthraquinone (16). Red needle crystals. Mps 220-221 °C. UVλ_{max} EtOH nm: 421, 278, 262, 231. UVλ_{max} EtOH/ -OH nm: 505, 314, 258. IR ν_{max} (KBr) cm⁻¹: 3467, 1653, 1637. MS m/z: 268 [M⁺], 239, 197, 169, 139, 115. ¹H NMR (CDCl₃, 300MHz): 13.20 (1H, s, 1-OH), 8.23 (1H, d, J=8.1, H-8), 8.12 (1H, s, H-5), 7.89 (1H, d, J=8.4, H-4), 7.61 (1H, d, J=8.1, H-7), 7.19 (1H, d, J=8.4, H-3), 4.04 (3H, s, 2-OCH₃), 2.56 (3H, s, 6-CH₃). ¹³C NMR (CDCl₃, 75.5 MHz): 189.1 (C=O, C-9), 181.8 (C=O, C-10), 154.0 (C-OH, C-1), 152.7 (C-OCH₃, C-2), 146.2 (C-6), 134.6 (C-7), 134.0 (C-11), 131.10 (C-12), 127.8 (C-5), 127.1 (C-8), 125.5 (C-14), 121.0 (C-4), 116.1 (C-13), 115.6 (C-3), 56.4 (2-OCH₃), 22.0 (6-CH₃)



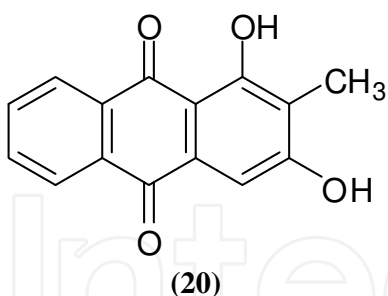
Lucidin- ω -methyl ether (**17**). Yellow crystals. Mps 175-179°C [lit 170 °C, Dictionary of Natural Products (1995); 163-166 °C, Leistner (1975)]. UV λ_{max} EtOH nm: 412, 280, 24. UV λ_{max} EtOH/ -OH nm: 491, 314, 242 IR ν_{max} (KBr) cm^{-1} : 3428, 2927, 1668, 162. MS m/z : 284 [M^+], 263, 241, 213, 185. ^1H NMR (CDCl_3 , 300MHz): 13.29 (1H, s, 1-OH), 9.39 (1H, s br, 3-OH), 8.27 (2H, m, H-5, H-8), 7.80 (2H, m, H-6, H-7), 7.32 (1H, s, H-4), 4.90 (2H, s, 2- CH_2OCH_3), 3.59 (3H, s, 2- CH_2OCH_3). ^{13}C NMR (CDCl_3 , 75.5 MHz): 186.9 (C=O, C-9), 182.2 (C=O, C-10), 164.1 (C-1), 161.7 (C-3), 134.1 (C-11), 134.1 (C-12), 133.6 (C-6), 133.5 (C-7), 126.8 (C-2), 114.4 (C-4), 109.7 (C-8), 109.7 (C-13), 109.6 (C-5), 109.6 (C-14), 68.9 (2- CH_2OCH_3), 59.3 (2- CH_2OCH_3)



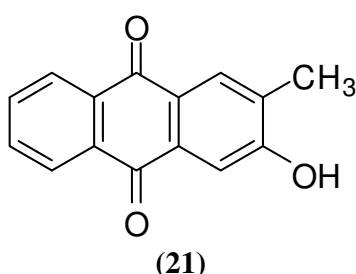
1,2-Dimethoxy-6-methyl-9,10-anthraquinone (**18**). Bright yellow crystals. Mps 193-196 °C. UV λ_{max} EtOH nm: 373, 341, 257, 222. UV λ_{max} EtOH/ -OH nm: 373, 342, 257, 222. IR ν_{max} (KBr) cm^{-1} : 1666, 1601, 1327, 1267 MS m/z : 282 [M^+], 253, 221, 194, 165, 139. ^1H NMR (CDCl_3 , 300MHz): 8.17 (2H, dd, $J=8.7, 7.8$, H-4, H-8), 8.06 (1H, s, H-5), 7.58 (1H, d, $J=7.8$, H-7), 7.28 (1H, d, $J=8.7$, H-3), 4.02 (6H, s, 1- OCH_3 , 2- OCH_3), 2.53 (3H, s, 6- CH_3). ^{13}C NMR (CDCl_3 , 75.5 MHz): 182.7 (C=O, C-9), 182.7 (C=O, C-10), 159.1 (C-1), 149.6 (C-2), 144.6 (C-6), 134.8 (C-7), 132.9 (C-11), 132.9 (C-12), 127.5 (C-14), 127.4 (C-13), 127.1 (C-8), 126.9 (C-5), 125.2 (C-4), 115.9 (C-3), 61.3 (1- OCH_3), 56.3 (2- OCH_3), 21.8 (6- CH_3)



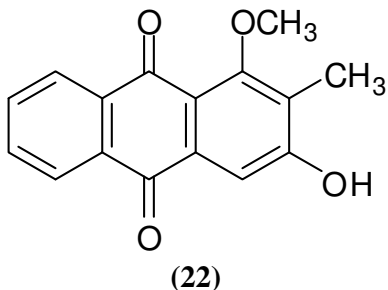
2-Hydroxy-3-methoxy-6-methyl-9,10-anthraquinone (**19**) Light yellow amorphous solid. Mp 210-215 °C. UV λ_{max} EtOH nm: 393, 286, 244. UV λ_{max} EtOH/ -OH nm: 509, 316, 250. IR ν_{max} (KBr) cm^{-1} : 3203, 2927, 2869, 1666, 1265. MS m/z : 268 (M^+), 239, 207, 169. ^1H NMR (CDCl_3 , 300MHz): 8.18 (1H, d, $J=8.1$, H-8), 8.08 (1H, s, H-5), 7.79 (1H, s, H-1), 7.76 (1H, s, H-4), 7.57 (1H, d, $J=8.1$, H-7), 6.23 (1H, s br, 2-OH), 4.11 (3H, s, 3- OCH_3), 2.54 (3H, s, 6- CH_3). ^{13}C NMR (CDCl_3 , 75.5 MHz): 182.4 (C=O), 162.8 (C-OH, C-2), 151.4 (C- OCH_3 , C-3), 144.9, 134.5, 133.6, 127.4, 127.2, 112.6, 108.3, 56.6 (3- OCH_3), 21.9 (6- CH_3)



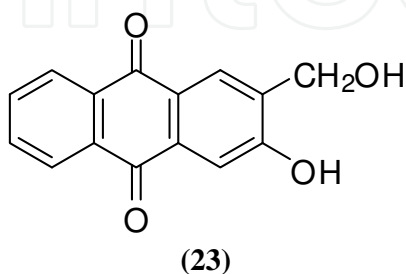
Rubiadin (**20**). Yellow crystals. Mps 250-258 °C [lit. 280-283 °C, Leistner (1975)]. $UV\lambda_{\max}$ EtOH nm: 413, 279. $UV\lambda_{\max}$ EtOH/ -OH nm: 496, 314, 241 IR ν_{\max} (KBr) cm^{-1} : 3436, 1653, 1626. MS m/z : 254 [M⁺], 226, 197, 152, 115. ^1H NMR (Acetone- d_6 , 300MHz): 13.20 (1H, s, 1-OH), 8.31 (1H, m, H-8), 8.23 (1H, m, H-5), 7.92 (2H, m, H-6, H-7), 7.38 (1H, s, H), 2.20 (3H, s, 2-CH₃). ^{13}C NMR (Acetone- d_6 , 75.5 MHz): 186.9 (C=O, C-9), 181.8 (C=O, C-10), 163.2 (C-OH, C-1), 162.4 (C-OH, C-3), 134.3, 134.2, 133.5, 133.5, 132.4, 126.8, 126.5, 117.9, 107.17, 7.3



3-Hydroxy-2-methyl-9,10-anthraquinone (**21**). Yellow crystals. Mps 138- 142 °C. $UV\lambda_{\max}$ EtOH nm: 379, 329, 274, 245, 239. $UV\lambda_{\max}$ EtOH/ -OH nm: 496, 314, 246 . IR ν_{\max} (KBr) cm^{-1} : 3436, 1663, 651. MS m/z 238 [M⁺], 238, 210, 181, 152, 105. ^1H NMR (Acetone- d_6 , 300MHz): 8.23 (2H, m, H-5, H-8), 8.05 (1H, s, H-1), 7.89 (2H, m, H-6, H-7), 7.67 (1H, s, H-4), 2.39 (3H, s, 2-CH₃). ^{13}C NMR (Acetone- d_6 , 75.5 MHz): 182.6 (C=O, C-10), 181.5 (C=O, C-9), 161.0 (C-OH, C-3), 134.1 (C-2), 133.8 (C-14), 133.7 (C-7), 133.6 (C-6), 132.2 (C-13), 130.1 (C-1), 126.6 (C-5), 126.5 (C-8), 111.4 (C-4), 15.6 (2-CH₃)



Rubiadin-1-methyl ether (**22**). Light yellow crystal. Mps 302-304 °C [282-284, Briggs (1976); 300 °C, Roberts (1977)]. $UV\lambda_{\max}$ EtOH nm: 354, 332, 279. $UV\lambda_{\max}$ EtOH/ -OH nm: 440, 314, 246. IR ν_{\max} (KBr) cm^{-1} : 3437, 2913, 2847, 1668, 1651. MS m/z : 268, 239, 207, 181. ^1H NMR (Acetone- d_6 , 300MHz): 9.50 (1H, s, br, 3-OH), 8.20 (2H, m, H-5, H-8), 7.87 (2H, m, H-6, H-7), 7.63 (1H, s, H-4), 3.90 (3H, s, 1-OCH₃), 2.27 (3H, s, 2-CH₃). ^{13}C NMR (Acetone- d_6 , 75.5 MHz): 182.7 (C=O), 180.4 (C=O), 161.2 (C-OH), 140.6, 134.4, 134.2, 133.0, 132.6, 126.8, 126.0, 60.4 (OCH₃), 8.4 (CH₃)



3-Hydroxy-2-hydroxymethyl-9,10-anthraquinone (**23**). Light yellow solid . $UV\lambda_{\max}$ EtOH nm: 374, 274, 238. $UV\lambda_{\max}$ EtOH/ -OH nm: 481, 311, 246 IR ν_{\max} (KBr) cm^{-1} : 3468, 1628. ^1H NMR (Acetone- d_6 , 300MHz): 8.38 (1H, s, H-4), 8.24 (2H, m, H-5, H-8), 7.89 (2H, m, H-6, H-7), 7.63 (1H, s, H-1), 4.803 (2H, s, 2-CH₂OH). ^{13}C NMR (Acetone- d_6 , 75.5 MHz): 182.9 (C=O, C-9), 181.7 (C=O, C-10), 160.1 (C-OH, C-3), 136.1 (C-2), 134.2 (C-14), 134.1 (C-11), 133.8 (C-6), 133.7 (C-7), 133.6 (C-12), 126.7 (C-4), 126.6 (C-5), 125.9 (C-13), 125.6 (C-8), 111.5 (C-1), 59.0 (2-CH₂OH)

Table 3.

which showed a 3J correlation with H-7. The methine carbons (C-3, C-4, C-5, C-7 and C-8) were assigned through HMQC correlations while the quaternary carbons (C-1, C-2, C-6, C-11, C-12, C-13 and C-14) were assigned based on careful analysis of HMBC spectrum. Both carbonyl carbons in this compound resonated very closely to each other with only 0.01 ppm difference at δ_C 182.70 and 182.71, which further confirmed the unchelated nature of the carbonyls. Presented below are structures and spectroscopic data of the isolated compounds.

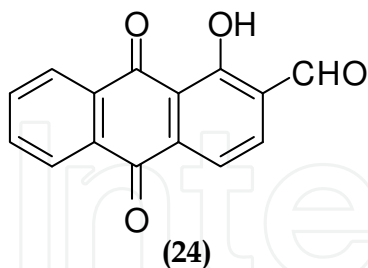
3.2 Anthraquinones of *Morinda elliptica*

Morinda elliptica or locally known as 'mengkudu kecil' is a shrub or small tree and it is very common in wild state of Malay Peninsula and northwards Burma (Burkill, 1966). It can be seen growing wild in newly developed areas, bushes and lowland secondary forest throughout the peninsula. *M. elliptica* is very common and always available and mostly used by the Malays for medicinal purposes. Traditionally, different parts of the plant are used in various ways for a number of health problems and ailments. The leaves may be added to rice for loss of appetite and taken for headache, cholera, diarrhea and wounds. Sometimes a lotion is made and used for hemorrhoid and applied upon body after childbirth (Burkill, 1966). The extracts and anthraquinones isolated from *M. elliptica* were reported to possess wide spectrum of biological activities such as antioxidant (Ismail, *et al.*, 2002; Jasril, *et al.*, 2003), antimicrobial, anti-HIV and anticancer (Ali, *et al.*, 2000).

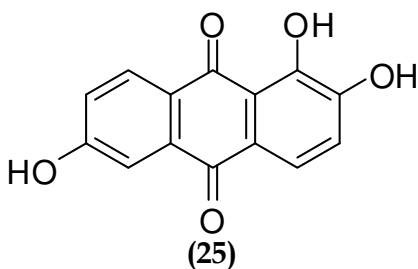


Fig. 5. *Morinda elliptica*

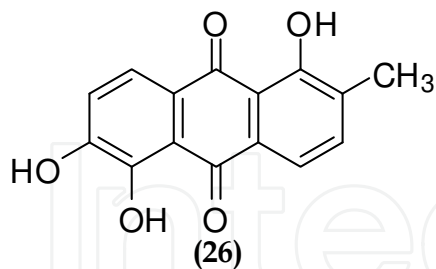
Five anthraquinones in roots of *M. elliptica* which are nordamnacanthal **13**, damnacanthal **15**, lucidin- ω -methyl ether **17**, rubiadin **20** and rubiadin-1-methyl ether **22** are the same constituents found in *R. elliptica*. The others are 1-hydroxy-2-methylanthraquinone **23**, soranjidiol **25**, morindone **26**, morindone-5-methyl ether **27** and alizarin-1-methyl ether **28**. In addition, 2-formyl-1-hydroxyanthraquinone **24** was reported as a new naturally occurring anthraquinone from roots of *M. elliptica*. HR-MS of **24** showed molecular ion peak at 252.0414 consistent with molecular formula of $C_{15}H_{14}O_4$. A bathchromic shift (407 to 531 nm) upon adding NaOH suggested the presence of OH at C-1 of the anthraquinone skeleton. The presence of hydroxyl group was evident from the broad stretching band observed at 3448 cm^{-1} . Two sharp stretching vibrations due to chelated and unchelated carbonyls were observed at 1638 and 1676 cm^{-1} , respectively. In the proton NMR, the signal for chelated hydroxyl group is at δ_H 13.26. The splitting pattern of 1H NMR suggest substitution pattern



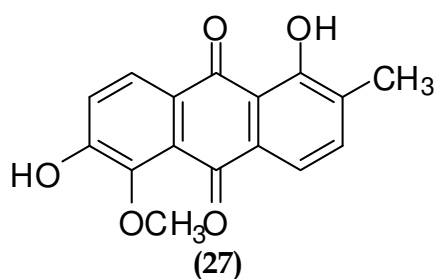
2-Formyl-1-hydroxy-9,10-anthraquinone (**24**). Mps 183-185 °C [lit. 259-260 °C, Rath et al. (1995)]. UV λ_{max} EtOH nm: 229, 278, 331, 407. UV λ_{max} EtOH/ -OH nm: 229, 280, 308, 531. IR ν_{max} (KBr) cm^{-1} : 3448 (OH), 1696 (aldehyde), 1676 (C=O unchelated), 1638 (C=O chelated), 1592 (C=C aromatic). MS m/z 252 (M^+), 2224, 196, 168. ^1H NMR (CDCl_3 , 500MHz): 13.26 (1H, s, 1-OH), 10.63 (1H, s, CHO), 8.35 (1H, m, H-8), 8.32 (1H, m, H-5), 8.23 (1H, d, J = 8.0 Hz, H-3), 7.89 (1H, d, J = 8.0 Hz, H-4), 7.88 (2H, m, H-6, H-7). ^{13}C NMR (CDCl_3 , 125 MHz): 164.5 (C-1), 128.4 (C-2), 135.4 (C-3), 118.7 (C-4), 127.7 (C-5), 134.7 (C-6), 135.3 (C-7), 127.2 (C-8), 188.9 (C-9), 181.8 (C-10), 117.4 (C-11), 137.2 (C-12), 134.8 (C-13), 133.3 (C-14) and 188.0 (C-15)



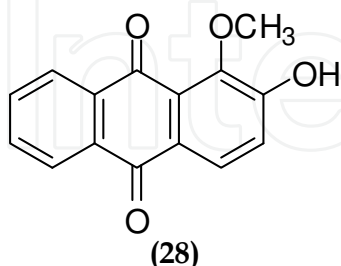
Soranjidiol. Yellow-orange needles (**25**) Mps 276-273 °C [lit. 271-272 °C, Adesogan (1973)]. UV λ_{max} EtOH nm: 265, 409. UV λ_{max} EtOH/ -OH nm: 308, 489. IR ν_{max} (KBr) cm^{-1} : 3401 (OH), 1667 (C=O unchelated), 1635 (C=O chelated), 1593 (C=C aromatic). MS m/z 254 (M^+), 226, 197, 115. ^1H NMR ($\text{DMSO}-d_6$, 500 MHz): 13.10 (1H, s, 1-OH), 11.21 (1H, s, 6-OH), 7.63 (1H, d, J = 7.57 Hz, H-3), 7.57 (1H, d, J = 7.57 Hz, H-4), 7.25 (1H, dd, $J_{7,8}$ = 8.55 Hz, $J_{7,5}$ = 2.69 Hz, H-7), 7.45 (1H, d, J = 2.69 Hz, H-5), 2.27 (3H, s, CH_3). ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz): 187.6 (C=O), 181.8 (C=O), 163.8 (C-OH), 160.0 (C-OH), 136.9, 135.6, 134.2, 131.1, 129.8, 124.5, 121.4, 118.6, 114.7, 112.5, 15.8 (CH_3)



Morindone (**26**). Orange needles. Mps 240-241 °C (CHCl_3) [lit. 248-249.5 °C, Leistner (1975)]. UV λ_{max} EtOH nm: 260, 299, 448. UV λ_{max} EtOH/ -OH nm: 260, 302, 338, 558. IR ν_{max} (KBr) cm^{-1} : 3462 (OH), 1628 (C=O chelated). MS m/z 270 (M^+), 242, 135. ^1H NMR (CDCl_3 , 500MHz): 13.21 (1H, s, 1-OH), 12.95 (1H, s, 5-OH), 7.85 (1H, d, J = 8.2 Hz, H-8), 7.75 (1H, d, J = 7.7 Hz, H-4), 7.52 (1H, d, J = 7.6 Hz, H-3), 7.26 (1H, d, J = 8.2 Hz, H-7), 6.32 (1H, s, 6-OH), 2.39 (3H, s, CH_3). ^{13}C NMR (CDCl_3 , 125 MHz): 186.6 (C=O), 179.9 (C=O), 170.4 (C-OH), 169.8 (C-OH), 161.4 (C-OH), 151.3, 149.4, 136.6, 130.9, 121.3, 119.8, 118.9, 115.3, 16.3 (CH_3)



Morindone-5-methyl ether (**27**). Orange crystals. Mp 232 °C [lit. 223 °C, Chang & Lee (1984)]. UV λ_{max} EtOH nm: 410, 497. UV λ_{max} EtOH/ -OH nm: 314, 388, 498. IR ν_{max} (KBr) cm^{-1} : 3389 (OH), 2926, 1672 (C=O unchelated), 1630 (C=O chelated), 1581 (C=C aromatic). MS m/z 284 (M^+), 266, 238, 197. ^1H NMR (CDCl_3 , 500MHz): 13.02 (1H, s, 1-OH), 8.14 (1H, d, J = 8.55 Hz, H-8), 7.70 (1H, d, J = 8.06 Hz, H-4), 7.51 (1H, d, J = 7.81 Hz, H-3), 7.35 (1H, d, J = 8.54 Hz, H-7), 6.73



(1H, s, 6-OH), 4.03 (3H, s, OCH₃), 2.37 (3H, s, CH₃). ¹³C NMR (CDCl₃, 125 MHz): 187.8 (C=O), 182.0 (C=O), 160.6 (C-OH), 155.9, 146.8, 136.9, 134.5, 132.3, 127.1, 125.9, 125.5, 112.0, 118.9, 114.7, 62.3 (OCH₃), 16.1 (CH₃)

Alizarin-1-methyl ether. Yellow-orange crystals (28). Mp 164 [lit 178-179°C, Chang & Lee (1984)]. UVλ_{max} EtOH nm: 313, 378, 485. UVλ_{max} EtOH/ -OH nm: 315, 333, 493. IR ν_{max} (KBr) cm⁻¹: 3443 (OH), 2926, 1671 (C=O unchelated), 1589 (C=C) aromatic. MS m/z 254 (M⁺), 236, 208, 183. ¹H NMR (DMSO-d₆, 500MHz): 8.28 (2H, m, H-5, H-8), 8.15 (1H, d, J = 8.55 Hz, H-4), 7.78 (2H, m, H-7, H-6), 7.37 (1H, d, J = 8.54 Hz, H-3), 6.70 (1H, s, 2-OH), 4.04 (3H, s, OCH₃). ¹³C NMR (DMSO-d₆ 125 MHz): 182.7 (C=O), 182.1 (C=O), 155.5, 146.6, 131.4, 133.9, 132.9, 127.5, 127.1, 126.8, 125.8, 125.6, 120.2, 62.3 (OCH₃)

on ring C only. H-3 and H-4 appeared as doublets at δ_H 8.23 and 7.89 respectively. A formyl group (δ_H 10.63) is attached to C-2. HMBC correlations of C-10 with H-3 and H-5 confirmed the assignment of the protons at their respective positions and supported by their respective COSY correlations. ¹³C NMR showed fifteen carbons peaks as expected. One of the chelated carbonyl carbon was further downfield at δ_C 188.9 (C-9), confirming the chelated nature of this carbonyl. The assignment of carbons were accomplished using FGHMQC and FGHMBC experiment. Presented below are structures and spectroscopic data of the isolated compounds.

4. Conclusion

The phytochemical study on *Fissistigma latifolium* and *Meiogyne virgata* (Annonaceae) yielded twelve alkaloids; (-)-*N*-methylguattescidine **1**, liriodenine **2**, lanuginosine **3**, (-)-asimilobine **4**, dimethyltryptamine **5**, (-)-remerine **6**, (-)-anonaine **7**, columbamine **8**, lysicamine **9**, norruciferine **10**, norushinsunine **11** and cleistopholine **12**. Tryptamine alkaloids have never been reported from *Fissistigma* species, whereas (-)-*N*-methylguattescidine **1** represents a rare finding of a naturally occurring 6a-methylated-7-oxo-aporphine alkaloid. Alkaloids **3**, **6**, **9** and **10** have never been reported from *Meiogyne* species.

Rennellia and *Morinda* are often confused with each other due to their similar traditional usage. Both plants are traditionally used for fever, postpartum and body ache treatment. Our phytochemical study on roots extract of *R. elliptica* showed significant similarities of major anthraquinones with those found in *Morinda* species. The major constituents of *R. elliptica*, nordamnacanthal, damnacanthal, rubiadian, rubiadin methyl ether and lucidin-ω-methyl ether are also present in *M. elliptica* and *M. citrifolia*.

5. Acknowledgment

Universiti Teknologi MARA, Universiti of Malaya, Ministry of Higher Education for Research grants and Ministry of Science, Technology and Innovation Malaysia for scholarship awarded to Alias,A.

6. References

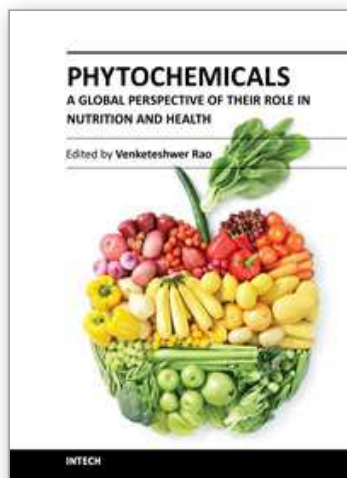
- Abd Aziz, R. (2003). *Siri Syarahan Perdana Professor*. Skudai: Universiti Teknologi Malaysia.
- Adesogan, E.K. (1973). Anthraquinones and anthraquinols from *Morinda lucida*. The biological significance of oruwal and oruwalol, *Tetrahedron* 29 (1973), p. 4099.
- Ahmad, R., Mahbob, E. N. M., Noor, Z. M., Ismail, N. H., Lajis, N. H., & Shaari, K. (2010). Evaluation of antioxidant potential of medicinal plants from Malaysian Rubiaceae (subfamily Rubioideae). *African Journal of Biotechnology*, 9(46), 7948-7954.
- Ahmad, R., Shaari, K., Lajis, N. H., Hamzah, A. S., Ismail, N. H., & Kitajima, M. (2005). Anthraquinones from *Hedyotis capitellata*. *Phytochemistry*, 66(10), 1141-1147.
- Ali, A. M., Ismail, N. H., Mackeen, M. M., Yazan, L. S., Mohamed, S. M., Ho, A. S. H., et al. (2000). Antiviral, Cytotoxic and Antimicrobial Activities of Anthraquinones Isolated from the Root of *Morinda elliptica*. *Pharmaceutical Biology*, 38, 298-301.
- Alias, A., Hazni, H., Mohd Jaafar, F., Awang, K. and Ismail, N. H. (2010). Alkaloids from *Fissistigma latifolium* Dunal Merr. *Molecules*, 15, 4583-4588.
- Awang, K.; Hamid, A.; Hadi, A. (2000). Protoberberine Alkaloids From *Fissistigma fulgens* Merr. (Annonaceae). *Malaysian J. Sci.*, 19, 41-44.
- Briggs, L.H., Beachen, J.F., Cambie, R.C., Dudman, N.P.B., Steggles, A.W. & Rutledge, P.S. (1976) Chemistry of *Coprosma* genus. Part XIV. Constituents of five New Zealand species. *J. Chem. Soc. Perkin Trans. I*, 1789-1792
- Burkill, I. H. (1966). *A Dictionary of the Economic Product of the Malay Peninsular*. Volumes I & II. Ministry of Agriculture and Cooperatives, Kuala Lumpur.
- Chan, K. C. & Toh, H. T. (1985). A new aporphinoid from *Desmos dasymachallus*. In: *Proceedings of the 2nd Meeting of the Natural Products Group*, edited by Said, I.M. & Zakaria, Z. 17-20. Jabatan Kimia, Fakulti Fizis dan Gunaan, Universiti Kebangsaan Malaysia, Bangi.
- Chang, P. and Lee, K., Cytotoxic antileukemic anthraquinones from *Morinda parvifolia*. *Phytochemistry*, 23, 1733-1736. (1984).
- Connolly, J. D., Haque, M. D. E., Kadir, A. A. (1996): Two 7,7-bisdehydroaporphine alkaloids from *Polyalthia bullata*. *Phytochemistry* 43: 295-297.
- Cordell, G.A. (1981). *Introduction to Alkaloid: A Biogenetic Approach*; John Wiley & Sons: New York, NY, USA, 6-19.
- Derksen, G. C. H., Van Beek, T. A., & Atta ur, R. (2002). *Rubia tinctorum* L *Studies in Natural Products Chemistry* (Vol. Volume 26, Part 7, pp. 629-684): Elsevier.
- Hamzah, A. S., & Lajis, N. H. (1998). Chemical Constituents of *Hedyotis herbaceae*. *ARBEC, Article II*, 1-6.
- Han, Y.-S., der Heiden, R. V., & Verpoorte, R. (2001). Biosynthesis of Anthraquinones in Cell Cultures of the Rubiaceae. *Plant Cell, Tissue and Organ Culture*, 67, 201-220.
- Hutchinson, J. (1973). *The Families of Flowering Plants* (3rd ed.): Oxford University Press.
- Ismail, N. H., Ali, A. M., Aimi, N., Kitajima, M., Takayama, H., & Lajis, N. H. (1997). Anthraquinones from *Morinda elliptica*. *Phytochemistry*, 45(8), 1723-1725.
- Ismail, N. H., Mohamad, H., Mohidin, A., & Lajis, N. H. (2002). Antioxidant Activity of Anthraquinones from *Morinda elliptica*. *Natural Product Science*, 8(2), 48-51.
- Jasril, Lajis, N. H., Lim, Y. M., Abdullah, M. A., Sukari, M. A., & Ali, A. M. (2003). Antitumor Promoting and Antioxidant Activities of Anthraquinones Isolated from the Cell

- Suspension Culture of *Morinda elliptica*. *Asia Pacific Journal of Molecular Biology and Biotechnology*, 11(1), 3-7.
- Kan, W. S. (1979). In *Pharmaceutical Botany*; National Research Institute of Chinese Medicine: Taiwan, 268.
- Kam, T. S. (1999). Alkaloids from Malaysian Flora, in *Alkaloids: Chemical and Biological Perspectives*, S. W. Pelletier (Ed.), Pergamon, Amsterdam, Volume 14, Chapter 2, 285-435.
- Kamaruddin, M. S. (1998). Proceedings Malaysian Traditional Medicine, 10-11 June 1998, Universiti Malaya, Kuala Lumpur, 80.
- Kong, J.-M., Goh, N.-K., & Chia, T.-F. (2003). Recent Advances in Traditional Plant Drugs and Orchids. *Acta Pharmacologica Sinica*, 24(1), 17-21.
- Lajis, N. H., Ahmad, R., & Atta-ur, R. (2006). Phytochemical studies and pharmacological activities of plants in genus *Hedyotis/oldenlandia* *Studies in Natural Products Chemistry* (Vol. Volume 33, Part 13, pp. 1057-1090): Elsevier.
- Lavault, M., Cabalion, P. and Bruneton, J. (1981). Alkaloids of *Uncaria guianensis*. *Planta Med.* 42, 50.
- Lee, H. H. (1969). Colouring matters from *Prismatomeris malayana*. *Phytochemistry*, 8(2), 501-503.
- Leistner, E. (1975). Isolation, identification and biosynthesis of anthraquinones in cell suspension cultures of *Morinda citrifolia*. *Planta Med.* (Suppl.) 214-224.
- Mat Salleh, K., & Latiff, A. (2002). *Tumbuhan Ubatan Malaysia*: Universiti Kebangsaan Malaysia & Kem, Sains, Teknologi dan Alam Sekitar.
- Nik Idris, Y., Lim, S. Y., Zaemah, J. and Ikram, M. S. (1994). *Alkaloid daripada Batang Fissistigma latifolium (Annonaceae) dan Potensinya Sebagai Dadah Anti-Leukaemia*, Laporan Teknik FSFG 4 : 199-204
- Osman, C. P., Ismail, N. H., Ahmad, R., Ahmat, N., Awang, K., & Jaafar, F. M. (2010). Anthraquinones with Antiplasmodial Activity from the Roots of *Rennellia elliptica* Korth. (Rubiaceae). *Molecules*, 15(10), 7218-7226.
- Parker, Sybil P. (1997). *Chemistry; Dictionaries*. McGraw-Hill (New York).
- Perry, L. M. (1980). *Medicinal Plants of Southeast Asia*. MIT: Cambridge, 19.
- Rath, G., Ndonzao, M., & Hostettmann, K. (1995). Antifungal Anthraquinones from *Morinda lucida*. *Int J. Pharmacogn.*, 33, 107-114.
- Roberts, J. L., Rutledge, P. S., and Trebilcock, M. J. (1977). Experiments Directed Towards the Synthesis of Anthracyclinones. I Synthesis of 2-Formylmethoxyanthraquinones *Aust. J. Chem.*, , 30, 1553.
- Saaïd M., and Awang, K. (2005) Alkaloids of *Fissistigma manubriatum*. *Malaysian Journal of Science*. 24 (1), 41-45.
- Sinclair, J., (1955) A revision of the Malayan Annonaceae. *The Gardens' Bulletin Singapore*, 14, 149-69.
- Tadic, D., Cassels, B. K., Leboeuf, M. and Cavé, A. (1987). Kinabaline and the aporphinoid biogenesis azaanthracene and azafluorene alkaloids. *Phytochemistry*, 26, 537-541.
- Teo, L.E., Pachiaper, G., Chan, K.C., Hadi, H.A., Weber, J.F., Deverre, J.R., David, B. & Sevenet, T. (1990). A new phytochemical survey of Malaysia V. Preliminary screening and plant chemical studies. *J. Ethnopharmacol.* 28(1) : 63-101.
- Verdout, B. (1976). *Annonaceae, Flora of Tropical East Africa*; Crown Agents for Oversea Government and Administrations: London, UK, pp. 101-102.

Wong, K. M. (1989). Rubiaceae (from the genus *Rubia*). In F. S. P. Ng (Ed.), *Tree Flora of Malaya; A Manual for Foresters* (Vol. 4, pp. 324-337, 404-405): Longman Malaysia.

IntechOpen

IntechOpen



Phytochemicals - A Global Perspective of Their Role in Nutrition and Health

Edited by Dr Venketeshwer Rao

ISBN 978-953-51-0296-0

Hard cover, 538 pages

Publisher InTech

Published online 21, March, 2012

Published in print edition March, 2012

Phytochemicals are biologically active compounds present in plants used for food and medicine. A great deal of interest has been generated recently in the isolation, characterization and biological activity of these phytochemicals. This book is in response to the need for more current and global scope of phytochemicals. It contains chapters written by internationally recognized authors. The topics covered in the book range from their occurrence, chemical and physical characteristics, analytical procedures, biological activity, safety and industrial applications. The book has been planned to meet the needs of the researchers, health professionals, government regulatory agencies and industries. This book will serve as a standard reference book in this important and fast growing area of phytochemicals, human nutrition and health.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Nor Hadiani Ismail, Asmah Alias and Che Puteh Osman (2012). Alkaloids and Anthraquinones from Malaysian Flora, *Phytochemicals - A Global Perspective of Their Role in Nutrition and Health*, Dr Venketeshwer Rao (Ed.), ISBN: 978-953-51-0296-0, InTech, Available from: <http://www.intechopen.com/books/phytochemicals-a-global-perspective-of-their-role-in-nutrition-and-health/alkaloids-and-anthraquinones-from-malaysian-flora>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen